IB/05/00148

सत्यमेव जयते

INTELLECTUAL PROPERTY **INDIA**

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY
PATENT OFFICE, DELHI BRANCH
W - 5, WEST PATEL NAGAR
NEW DELHI - 110 008.

I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application*** *and* ***Complete Specification*** *filed in connection with Application for Patent No.* ***127/Del/2004*** *dated* ***23rd January 2004.***

Witness my hand this 22nd day of February 2005.

(S.K. PANGASA)
Assistant Controller of Patents & Designs

PRIORITY DOCUMENT
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0127 DEL 04

23 JAN 20

FORM 1

THE PATENTS ACT, 1970

(39 of 1970)

APPLICATION FOR GRANT OF A PATENT

(See Sections 5(2), 7, 54 and 135; and rule 39)

1 We, **RANBAXY LABORATORIES LIMITED**, a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled **"STABLE ORAL PHARMACEUTICAL COMPOSITIONS OF CANDESARTAN CILEXETIL"**

(b) that the Complete Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. ROMI BARAT SINGH

b. GIRISH KARANTH K

c. VISHNUBHOTLA NAGA PRASAD

d. SANJEEV KUMAR SETHI

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon – 122001 (Haryana), India, all Indian Nationals.

4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows: **NOT APPLICABLE**

5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which we are the applicant: **NOT APPLICABLE**

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application deemed to have been filed on ..... Under section 16 of the Act. **NOT APPLICABLE**

7. That we are the assignee or legal representatives of the true and first inventors.

8. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18, Udyog Vihar Industrial Area,
Gurgaon – 122001 (Haryana). INDIA.
Tel. No. (91-124) 2343126, 2342001-10; 5012501-10

Following declaration was given by the inventors or applicants in the convention country:

We, ROMI BARAT SINGH, GIRISH KARANTH K, VISHNUBHOTLA NAGA PRASAD, SANJEEV KUMAR SETHI of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention or applicant in the convention country declare that the applicant herein, **Ranbaxy Laboratories Limited**, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representatives.

a. Romi Singh
(ROMI BARAT SINGH)

b.
(GIRISH KARANTH K)

c. V. Nagaprasad
(VISHNUBHOTLA NAGA PRASAD)

d.
(SANJEEV KUMAR SETHI)

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Followings are the attachment with the application:
    a. Complete Specification (3 copies)
    b. Drawings (3 copies)
    c. Priority document(s)
    d. Statement and Undertaking on FORM – 3
    e. Power of Authority (Not required)
    f. Fee Rs.**3,000**/- (Rupees Three Thousand only..) in cheque bearing No. dated : drawn on HDFC Bank, New Delhi.

We request that a patent may be granted to us for the said invention.

Dated this **23RD** day of **January, 2004.**

For Ranbaxy Laboratories Limited

(SUSHIL KUMAR PATAWARI)
Company Secretary

0127 DEL 04

23 JAN

FORM 2

The Patents Act, 1970

(39 of 1970)

COMPLETE SPECIFICATION

(See Section 10)

STABLE ORAL PHARMACEUTICAL COMPOSITIONS OF CANDESARTAN CILEXETIL

RANBAXY LABORATORIES LIMITED

19, NEHRU PLACE, NEW DELHI - 110019

A Company incorporated under the Companies Act, 1956.

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

The present invention relates to stable oral pharmaceutical compositions of Candesartan Cilexetil.

In the field of therapy of hypertension, angiotensin II receptor antagonist has attracted attention as an effective agent for the therapy of hypertension following angiotensin I converting enzyme (ACE) inhibitor. Candesartan is a selective AT_1 subtype angiotensin II receptor antagonist. Candesartan Cilexetil is a prodrug and is hydrolyzed to candesartan during absorption from the gastrointestinal tract. It falls in the class of benzimidazole -7- carboxylic acid and its derivatives thereof. These agents exhibit a strong and more effective hypotensive action and are less likely to cause coughing as side effect as compared to other class of ACE inhibitors.

Candesartan Cilexetil is stable against temperature, moisture and light when it is alone in the solid state, however when it is prepared into tablets with other formulation and incorporated with other ingredients, it has been observed that lowering of the content of the active ingredient has been observed with the lapse of time.

US Pat No 5,534,534 discloses that the reduction in the content of the Candesartan Cilexetil with the lapse of time, in pharmaceutical compositions can be reduced by incorporating oily substances having a low melting point in these compositions. This oily substance having a lower melting point is incorporated into the active component to form a stable composition in which decomposition with time caused by compression can be suppressed. Thus resulting in a stable composition in which the crystalline disorder is minimized.

The stability of pharmaceutical compositions of Candesartan Cilexetil can also be correlated to various degradation products like desethyl candesartan and also total related substances. The increase in the levels of desethyl candesartan and total related substances is a result of an unstable / less stable formulation

The present invention is directed to a surprising and unexpected discovery of use of fatty substances to form a stable pharmaceutical composition of Candesartan Cilexetil

with respect to the levels of impurities in particular desethyl candesartan and consequently total related substances.

Fatty substances usable in the present invention can be selected from Lipids and Phospholipids or mixtures thereof.

Hence the present invention provides an economical method of stabilization of Candesartan Cilexetil. The present invention also enhances the shelf life of the product through improved stability of the composition.

Hence in one aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance selected from Lipids and Phospholipids or the mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and Lipids selected from fatty acids such as lauric acid, myristic acid, stearic acid, palmitoleic acid, oleic acid,capric acid, caprylic acid, oleic acid, linoleic acid, arachidonic acid or mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and Lipids selected from fatty acid esters such as glycerol stearate, glycerol palmitate, glyceryl caprate, glyceryl caprylate, glyceryl caprylate/caprate, glycerol oleate, glycerol linoleate, glyceryl lauropalmitooleate or mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and Phospholipids selected from phosphoglycerides such as lecithin, cephalin, soyalecithin, egglecithin , phosphatidylserine, phosphatidyl-inositol or mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and Phospholipids selected from sphingolipids. In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil and a fatty substance wherein the concentration of Candesartan Cilexetil is the range of **2% to 35%w/w** and the fatty substance is in the range of **0.5% to 10%w/w** of the total weight of the composition.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil in combination with at least one other active agent and a fatty substance.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil in combination with at least one other active agent and a fatty substance wherein the fatty substance is selected from Lipids and Phospholipids or mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil in combination with at least one other active agent selected from the group consisting of diuretics, sympathoplegic agents, vasodilators, ACE inhibitors and angiotensin receptor antagonist in each case in free form or in form of a pharmaceutically acceptable salt and a fatty substance wherein fatty substance is selected from Lipids and Phospholipids or mixtures thereof.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil in combination with at least one other active agent selected from the group consisting of diuretics, sympathoplegic agents, vasodilators, ACE inhibitors and angiotensin receptor antagonist in each case in free form or in form of a pharmaceutically acceptable salt thereof and a fatty substance wherein the concentration of Candesartan Cilexetil is the range of 2% to 35%w/w and the fatty substance is in the range of 0.5% to 10%w/w of the total weight of the composition.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising effective amount of Candesartan Cilexetil and a fatty substance for the preparation of a medicament for the treatment of hypertension.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil and a fatty substance selected from Lipids and Phospholipids or mixtures thereof; for the preparation of a medicament for the treatment of hypertension; wherein the concentration of Candesartan Cilexetil is the range of **2% to 35%w/w** and the fatty substance is in the range of **0.5% to 10%w/w** of the total weight of the composition.

In another aspect it provides a stabilized pharmaceutical composition for oral use comprising Candesartan Cilexetil in combination with at least one other active agent and a fatty substance selected from Lipids and Phospholipids or the mixtures thereof for the preparation of a medicament for the treatment of hypertension; wherein the concentration of Candesartan Cilexetil is the range of **2% to 35%w/w** and the fatty substance is in the range of **0.5% to 10%w/w** of the total weight of the composition.

In another aspect it provides a process for preparation of stabilized pharmaceutical composition for oral use comprising effective amount of Candesartan Cilexetil and a fatty substance.

The term 'Candesartan Cilexetil' used herein refers to a prodrug that is hydrolyzed to Candesartan during absorption from the gastrointestinal tract.

The term 'stabilized pharmaceutical composition' relates to a composition capable of maintaining excellent stability with respect to the levels of impurities especially Desethyl candesartan and consequently total related substances.

The stabilizing agent is selected from fatty substances selected from Lipids and Phospholipids or the mixtures thereof.

Lipids can be selected from fatty acids and fatty acid esters.

Examples of fatty acids include lauric acid, myristic acid, stearic acid, palmitoleic acid, oleic acid, capric acid, caprylic acid, oleic acid, linoleic acid, arachidonic acid or mixtures thereof.

Examples of fatty acid esters include glycerol stearate, glycerol palmitate, glyceryl caprate, glyceryl caprylate, glyceryl caprylate/caprate, glycerol oleate, glycerol linoleate, glyceryl lauropalmitooleate or mixtures thereof.

Phospholipids can be selected from phosphoglycerides and sphingolipids.

Examples of Phosphoglycerides include lecithin, cephalin, soyalecithin, egglecithin , phosphatidylserine, phosphatidyl-inositol or mixtures thereof.

These substances may be used alone or in a mixture of two or more.

The composition may contain other pharmaceutically acceptable excipients in addition to Candesartan Cilexetil and fatty substance.

The pharmaceutical composition can be prepared by processes known in the prior art such as wet granulation, dry granulation or direct compression and the final dosage form may be in the form of tablets or capsules.

In one of the embodiments Candesartan Cilexetil tablet may be prepared by dispersing Candesartan Cilexetil and fatty substance in the binder solution; granulating filler and disintegrant with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

In another embodiment Candesartan Cilexetil tablet may be prepared by dispersing Candesartan Cilexetil, fatty substance and a part of filler in binder solution; granulating remaining quantity of filler and disintegrant with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

In another embodiment Candesartan Cilexetil tablet may be prepared by dispersing Candesartan Cilexetil, fatty substance and a part of disintegrant in the binder solution; granulating remaining quantity of disintegrant and filler with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

The term 'other pharmaceutically acceptable excipient' refers to ingredients of the composition, excluding the active drug substance.

Examples of other pharmaceutically acceptable excipients as used herein include fillers, binders, disintegrants, lubricants, glidants, colors and the like.

The fillers can be selected from the group comprising of corn starch, lactose, white sugar, sucrose, sugar compressible, sugar confectioners, glucose, sorbitol, calcium carbonate, calcium phosphate-dibasic, calcium phosphate-tribasic, calcium sulfate, microcrystalline cellulose, silicified microcrystalline cellulose, cellulose powdered, dextrates, dextrins, dextrose, fructose, kaolin, lactitol, mannitol, sorbitol, starch, starch pregelatinized and the like.

Examples of binders include methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, gelatin, gum Arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, and the like.

Examples of disintegrants include calcium carboxymethyl cellulose, colloidal silicon dioxide, starch, croscarmellose sodium, crospovidone, sodium starch glycolate and the like.

Examples of lubricants and glidants include colloidal anhydrous silica, stearic acid, magnesium stearate, calcium stearate, talc, hydrogenated castor oil, sucrose esters of fatty acids, microcrystalline wax, yellow beeswax, white beeswax and the like.

The coloring agents of the present invention may be selected from any FDA approved colors for oral use.

Candesartan Cilexetil can be present in the range of **2% to 35%w/w** and most preferably about **3% to about 30% (w/w),** based on the total weight of the composition.

The fatty substance can be present in the range of **0.5% to 10%w/w** and most preferably about **1% to about 5% (w/w),** based on the total weight of the composition.

The tablets prepared by the present invention may be coated with one or more additional layers comprising film forming agents and/or pharmaceutically acceptable excipients.

The coating layers over the tablet may be applied as solution/ dispersion of coating ingredients using any conventional technique known in the prior art such as spray coating in a conventional coating pan or fluidized bed processor; dip coating and the like.

Example of solvents used for preparing a solution/dispersion of the coating ingredients include methylene chloride, isopropyl alcohol, acetone, methanol, ethanol, water and the like and mixtures thereof.

Example of film forming agents include ethyl cellulose, Hydroxypropyl methylcellulose, Hydroxypropyl cellulose, methyl cellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropyl methyl phthalate, cellulose acetate, cellulose acetate trimelliatate, cellulose acetate phthalate; Waxes such as polyethylene glycol; methacrylic acid polymers such as Eudragit ® RL and RS;

and the like and mixture thereof. Alternatively, commercially available coating compositions comprising film-forming polymers marketed under various trade names, such as Opadry may also be used for coating.

The following examples are illustrative of the invention, and are not to be construed as limiting the invention.

EXAMPLE 1

Ingredient	**Example 1 (wt/tablet) mg**
Intragranular ingredients	
Candesartan Cilexetil	32.12
Glyceryl caprate	8.00
Lactose monohydrate	265.88
Starch	67.00
Hydroxypropyl Cellulose	12.00
Calcium carboxymethyl cellulose	6.50
Purified Water	q.s
Extragranular ingredients	
Calcium carboxymethyl cellulose	6.50
Magnesium stearate	2.00

PROCEDURE:

1. Candesartan Cilexetil and Glyceryl caprate are dispersed in a solution of hydroxy propyl cellulose in water.
2. Lactose, starch, and a part of calcium carboxymethyl cellulose are mixed in a high shear mixer are granulated with the dispersion of Step 1.
3. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to sizing.
4. The remaining part of calcium carboxymethyl cellulose is passed through a screen and blended with the granules of step 3.
5. The magnesium stearate is passed through a screen, blended with the blend of step 4 and the total mixture is compressed to tablets.

EXAMPLE 2

Ingredient	Example 2 (wt/tablet) mg
Intragranular ingredients	
Candesartan Cilexetil	32.12
Glyceryl caprylate	8.00
Lactose monohydrate	250.88
Microcrystalline cellulose	67.00
Hydroxypropyl Cellulose	12.00
Calcium carboxymethyl cellulose	10.00
Colloidal silicon dioxide	8.00
Purified Water	q.s
Extragranular ingredients	
Calcium carboxymethyl cellulose	10.00
Magnesium stearate	2.00

PROCEDURE:

1. Candesartan Cilexetil, Glyceryl caprylate and part of lactose are dispersed in a solution of hydroxy propyl cellulose in water.
2. The remaining part of lactose, microcrystalline cellulose, a part of calcium carboxymethyl cellulose, and colloidal silicon dioxide are mixed in a high shear mixer are granulated with the dispersion of Step 1.
3. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to sizing.
4. The remaining quantity of calcium carboxymethyl cellulose is passed through a screen and blended with the granules of step 3.
5. The magnesium stearate is passed through a screen, blended with the blend of step 4 and the total mixture is compressed to tablets.

EXAMPLE 3

Ingredient	Example 3 (wt/tablet) mg
Intragranular ingredients	
Candesartan Cilexetil	32.12
Soyalecithin	8.00
Lactose monohydrate	250.88
Starch	67.00
Hydroxypropyl Cellulose	12.00
Calcium carboxymethyl cellulose	10.0
Colloidal silicon dioxide	8.0
Purified Water	q.s
Extragranular ingredients	
Calcium carboxymethyl cellulose	10.00
Magnesium stearate	2.00

PROCEDURE:

1. Candesartan Cilexetil, soyalecithin and part of calcium carboxymethyl cellulose are dispersed in a solution of hydroxy propyl cellulose in water.
2. The starch, lactose, colloidal silicon dioxide and, are mixed in a high shear mixer are granulated with the dispersion of Step 1.
3. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to sizing.
4. The remaining part of calcium carboxymethyl cellulose is passed through a screen and blended with the granules of step 3.
5. The magnesium stearate is passed through a screen, blended with the blend of step 4 and the total mixture is compressed to tablets.

Fatty substances show a stabilizing effect on Candesartan Cilexetil. Table 1 shows comparative stability data at various intervals (40ºC/75%RH) with reference to the amount of Desethyl Candesartan and total related substances found.

Table 1:

	Batch without stabilizer		Batch with Glyceryl caprate as stabilizer (Example 1)		Batch with soyalecithin as stabilizer (Example 3)	
	Initial	1M	Initial	1M	Initial	1M
Desethyl Candesartan (% w/w)	0.363	0.845	0.061	0.153	0.122	0.251
Total RS (% w/w)	1.342	2.524	0.821	1.000	0.861	1.334

Table 1 clearly indicates that the use of Fatty substances stabilizes the Candesartan Cilexetil compositions.

While there has been shown and described what are the preferred embodiments of the invention, one skilled in the pharmaceutical formulation art will appreciate that various modifications in the formulations and process can be made without departing from the scope of the invention as it is defined by the appended claims.

WE CLAIM:

1. A stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance.

2. The stabilized pharmaceutical composition according to claim 1 wherein the fatty substances are selected from lipids and phospholipids.

3. The stabilized pharmaceutical composition according to claim 2 wherein the lipids are selected from fatty acids and fatty acid esters.

4. The stabilized pharmaceutical composition according to claim 3 wherein the lipids are selected from fatty acids such as lauric acid, myristic acid, stearic acid, palmitoleic acid, oleic acid, capric acid, caprylic acid, oleic acid, linoleic acid, arachidonic acid or mixtures thereof.

5. The stabilized pharmaceutical composition according to claim 3 wherein the lipids are selected from fatty acid esters such as glycerol stearate, glycerol palmitate, glyceryl caprate, glyceryl caprylate, glyceryl caprylate/ caprate, glycerol oleate, glycerol linoleate, glyceryl lauropalmitooleate or mixtures thereof.

6. The stabilized pharmaceutical composition according to claim 5 wherein the fatty acid is glyceryl caprylate.

7. The stabilized pharmaceutical composition according to claim 5 wherein the fatty acid is glyceryl caprate.

8. The stabilized pharmaceutical composition according to claim 2 wherein the phospholipids are selected from phosphoglycerides and sphingolipids.

9. The stabilized pharmaceutical composition according to claim 8 wherein phospholipids are selected from phosphoglycerides such as lecithin, cephalin, soyalecithin, egglecithin, phosphatidylserine, phosphatidyl-inositol or mixtures thereof.

10. The stabilized pharmaceutical composition according to claim 9 wherein the phosphoglyceride is Soyalecithin.

11. The stabilized pharmaceutical composition according to claim 8 wherein phospholipids are selected from sphingolipids.

12. The stabilized pharmaceutical composition according to claim 1 wherein Candesartan Cilexetil is the range of **2% to 35%w/w** and the fatty substance is in the range of **0.5% to 10%w/w** of the total weight of the composition.

13. The stabilized pharmaceutical composition according to claim 1 wherein in addition to Candesartan Cilexetil and fatty substances, it comprises of other pharmaceutically acceptable excipients selected from a group consisting of filler, binder, disintegrant, lubricant, coloring and flavoring agent.

14. The stabilized pharmaceutical composition according to claim 13 wherein filler is selected from the group comprising of corn starch, lactose, white sugar, sucrose, sugar compressible, sugar confectioners, glucose, sorbitol, calcium carbonate, calcium phosphate-dibasic, calcium phosphate-tribasic, calcium sulfate, microcrystalline cellulose, silicified microcrystalline cellulose, cellulose powdered, dextrates, dextrins, dextrose, fructose, kaolin, lactitol, mannitol, sorbitol, starch, starch pregelatinized, sucrose, and mixtures thereof.

15. The stabilized pharmaceutical composition according to claim 14 wherein filler is lactose.

16. The stabilized pharmaceutical composition according to claim 14 wherein filler is microcrystalline cellulose.

17. The stabilized pharmaceutical composition according to claim 13 wherein binder is selected from methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, gelatin, gum arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, and the like.

18. The stabilized pharmaceutical composition according to claim 17 wherein binder is hydroxypropyl cellulose.

19. The stabilized pharmaceutical composition according to claim 13 wherein the disintegrant is selected from calcium carboxymethyl cellulose, colloidal silicon dioxide, starch, croscarmellose sodium, crospovidone, sodium starch glycolate and the like.

20. The stabilized pharmaceutical composition according to claim 19 wherein disintegrant is calcium carboxymethyl cellulose.

21. The stabilized pharmaceutical composition according to claim 19 wherein disintegrant is colloidal silicon dioxide.

22. The stabilized pharmaceutical composition according to claim 13 wherein lubricant is selected from colloidal anhydrous silica, stearic acid, magnesium stearate, calcium stearate, talc, hydrogenated castor oil, sucrose esters of fatty acids, microcrystalline wax, yellow beeswax, white beeswax and mixtures thereof.

23. The stabilized pharmaceutical composition according to claim 22 wherein lubricant is magnesium stearate.

24. The stabilized pharmaceutical composition according to claim 1 wherein the pharmaceutical composition is in the form of a tablet.

25. The stabilized pharmaceutical composition according to claim 1 wherein the pharmaceutical composition is in the form of capsule.

26. The stabilized pharmaceutical composition according to claim 24 wherein the tablet is further coated with one or more functional and/or non-functional layers.

27. A process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance by wet granulation.

28. The process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil according to claim 27 wherein in addition to Candesartan Cilexetil and a fatty substance, it also comprises of other pharmaceutically acceptable excipients.

29. The process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil according to claim 28 wherein other pharmaceutically acceptable excipients are selected from a group consisting of filler, binder, disintegrant, lubricant, coloring and flavoring agent.

30. The process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil according to claim 27, by dispersing Candesartan Cilexetil and fatty substance in the binder solution; granulating filler and disintegrant with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

31. The process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil according to claim 27, by dispersing Candesartan Cilexetil and fatty substance and a part of filler in binder solution; granulating remaining quantity of filler and disintegrant with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

32. The process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil according to claim 27, by dispersing Candesartan Cilexetil, fatty substance and a part of disintegrant in the binder solution; granulating remaining quantity of disintegrant and filler with the drug dispersion; drying the granules; sizing; lubricating and compressing the lubricated granules.

33. A process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance by dry granulation.

34. A process for preparation of stabilized pharmaceutical composition of Candesartan Cilexetil for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance by direct compression.

35. A medicament for the treatment of hypertension comprising an effective amount of Candesartan Cilexetil and a fatty substance.

36. A stabilized pharmaceutical composition for oral use comprising an effective amount of Candesartan Cilexetil and a fatty substance as described and illustrated herein.

Dated 23TH day of **January, 2004.**

For Ranbaxy Laboratories Limited

(Sushil Kumar Patawari)
Company Secretary

ABSTRACT

STABLE ORAL PHARMACEUTICAL COMPOSITIONS OF CANDESARTAN CILEXETIL

The invention relates to the use of fatty substances to form a stable pharmaceutical composition of Candesartan Cilexetil with respect to the levels of impurities in particular desethyl candesartan and consequently total related substances.